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REMARKS

Claims 1 and 3-30 are now pending. While the Office Action (under the Heading "Election/Restrictions") states that claims 14-26 are withdrawn as being directed to non-elected subject matter, Applicants understand the Examiner to have intended to withdraw claims 14-30 from further consideration. Claims 1, 5, 7 and 8 have been amended to correct obvious typographical errors and to more particularly point out and distinctly claim the subject matter Applicants regard as their invention. Claim 2 has been cancelled without prejudice or disclaimer.

Amendment or cancellation of any claim herein is not to be construed as acquiescence to any of the rejections/objections set forth in the instant Office Action, and was done solely to expedite prosecution of the application. Applicants make these amendments without prejudice to pursuing the original subject matter of this application in this application or a later filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject matter.

Support for the amendments can be found in the specification and claims as filed. No new matter has been added.

Double Patenting

Claims 1-10 and 13 are provisionally rejected under 35 U.S.C. §101 as claiming the same invention of claims 1-10 and 13 of co-pending application no. 10/367,105. Applicants note that the pending claims, as amended, are not identical to the claims now

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pending in co-pending application no. 10/367,105. However, if necessary, Applicants will address this provisional rejection when the claims are indicated to be allowable.

Rejection under 35 U.S.C. §112

Claims 1-10 and 13 stand rejected as failing to comply with the written description requirement. Applicants traverse.

Applicants submit that the claims as originally presented provide adequate written description such that one of ordinary skill in the art would appreciate the scope of the claimed subject matter. The subject compounds are described in terms of identifying characteristics (structural, physicochemical and functional). As described in the specification, including at pages 56-58 and Example 1, transportophores having the desired characteristics are readily identified by determination of their immune selectivity ratio coefficient (e.g., by the process described in Example 1) and their pKa. Thus, it would be readily ascertainable by one of ordinary skill in the art as to what an appropriate transportophore is.

Such "identifying characteristics" are considered to meet the requirements for written description. It is established that the "written description requirement for a claimed genus may be satisfied through a sufficient description of a representative number of species by actual reduction to practice ... or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties ..." (emphasis added). MPEP 2163(II)(A)(3)(a)(ii). In fact, Applicants have provided both representative examples and identifying physical and chemical properties in regard to their claimed transportophore containing compounds. The compounds are described as having characteristics including: (i) having an amphiphilic transportophore; (ii) having a transportophore with an immune selectivity ratio of at least 2; (iii) having a transportophore with a pKa of 6.5 to 9.5; and (iv) having an immune selectivity ratio of at least 2.

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Throughout the specification it is indicated that compounds having these characteristics, which are all readily ascertainable to one of ordinary skill in the art, provide the desired therapeutic bioavailability and improved efficacy relative to the transportophore and therapeutic agent individually. Moreover, representative examples are provided in the examples and the Tables that show diverse transportophore groups, linkers and structures useful in the claimed subject matter. As such, Applicants submit that their "description of a representative number of species by actual reduction to practice" and their "disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties" of the claimed subject matter satisfies the written description requirement as established and delineated in MPEP 2163.

Nonetheless in order to expedite prosecution, Applicants have amended claim 1 and cancelled claim 2. Claim 1 (and the remaining claims, all of which are directly or indirectly dependent thereon) recite compounds in which the transportophore is an amphiphilic moiety having an immune selectivity ratio of at least 2 and a pKa value of 6.5 to 9.5. Applicants submit that the pending claims meet the written description requirement for at least the aforementioned reasons. The dependent claims provide additional features of the claimed compounds. Claims 9 and 10 have additional specific structural description, thus further meeting the written description requirement.

For at least the foregoing reasons, withdrawal of the rejection is proper and the same is requested.

Rejections under 35 U.S.C. §102(b)

Claims 1-10 and 13 stand rejected under 35 U.S.C. 102(b) as being anticipated by Krivan *et al.*, U.S. Patent No. 5,466,681 ("Krivan"). This rejection is traversed.

The Examiner states that Krivan discloses an erythromycin-sulfatide conjugate, but recognizes that Krivan is silent as to the immune selectivity ratio of the transportophores and compounds disclosed therein. However, the Examiner states that

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"the examiner believes that the erythromycin-sulfatide complex would meet the limitations as claimed." Applicants respectfully disagree.

First, Applicants submit that the conjugates disclosed by Krivan are intended to be used as anti-infective agents (see, e.g., Krivan at Column 1, lines 38-40). In the erythromycin-sulfatide complex of Krivan, the sulfatide moiety is intended by Krivan to be a microorganism receptor, for increasing specificity for a pathogen (see, e.g., Krivan at Column 2, lines 8-20). The erythromycin component is not intended by Krivan to be a transportophore, as required by the pending claims, but rather a therapeutic (antibiotic) agent. In contrast, according to the pending claims, the therapeutic agent component of the compounds of the invention (component C) must be a *non-antibiotic* therapeutic agent.

Second, as the Examiner is apparently aware, sulfatides are saccharide-containing compounds. Such compounds are not generally capable of passive entry into cells, and will likely enter cells, if at all, via a specific transport mechanism, although it has been reported that sulfatides can be endocytosed by macrophages (see, e.g., Greenspan P, Gutman RL. *J Leukoc Biol.* (1994) 55(1):99-104).

As recited in pending claim 1, the compounds of the invention have an immune selectivity ratio of at least 2. As described in the present specification (see, e.g., page 32, lines 5-9), the immune selectivity ratio is the ratio of the concentration of a compound in immune cells to the concentration of the compound in erythrocytic cells after the compound has been incubated in a mixture of blood cells including erythrocytes.

It has been reported that sulfatides are bound to adhesive glycoproteins on the surface of red blood cells (see, e.g., Roberts DD and Ginsburg V., *Arch Biochem Biophys.* (1988) 267(2):405-15). Thus, it would be expected that a sulfatide-containing conjugate would be at least partially bound to the surface of red blood cells, rather than being concentrated in immune cells, when incubated in a mixture of blood cells including erythrocytes.

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In view of the foregoing, Applicants respectfully contend that the conjugates of Krivan would not have the claimed immune selectivity ratio, and therefore do not anticipate or render obvious the claimed compounds.

Claims 1-3, 5 and 13 stand rejected under 35 U.S.C. 102(b) as being anticipated by Liu *et al.*, U.S. Patent No. 5,928,868 ("Liu"). This rejection is traversed.

The Examiner states that Liu discloses macrolides coupled to steroids. The Examiner points specifically to Liu at Figure 7B for this proposition. However, the complex depicted in Figure 7B of Liu is a conjugate of dexamethasone with FK506; the Examiner apparently takes the position that FK506 is a transportophore.

The pending claims recite, *inter alia*, that the transportophore is an amphiphilic molecule having a pKa value of 6.5 to 9.5. Applicants point out that the pKa of FK506 (if a pKa can even be measured in aqueous solution for this compound) would not be in the claimed range of 6.5 to 9.5. Indeed, a theoretical pKa for FK506 (calculated using a commercially-available algorithm) is 9.96, which is outside the claimed pKa range. Alternatively, if the Examiner takes the position that dexamethasone is a transportophore according to Liu, Applicants submit that the pKa of dexamethasone also would not be within the claimed range. Therefore, the compounds of Liu cannot and do not anticipate or render obvious any of the pending claims.

For at least the foregoing reasons, withdrawal of the rejections under 35 U.S.C. 102(b) is proper and the same is requested.

Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is

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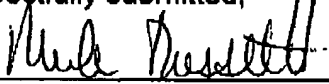
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respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call Applicants' undersigned representative to discuss the application. Applicants thank the Examiner in advance for this courtesy.

The undersigned requests any extension of time necessary for response. The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. (50551) 60636.

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Respectfully submitted,

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